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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/061,699	05/12/93	WEINER	A 0938.001

SCHWADRON EXAMINER

18N1/1106

KENNETH M. GOLDMAN
CHIRON CORP.
4560 HORTON ST., R-440
EMERYVILLE, CA 94608

ART UNIT	PAPER NUMBER
1816	27

DATE MAILED: 11/06/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 8/1/95 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-39 are pending in the application.
   Of the above, claims 13-39 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-12 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. Claims 1-12 are under consideration. Claims 1 and 7 have been amended.

RESPONSE TO APPLICANT'S ARGUMENTS

16. The use of the trademarks TRITON X-100, TWEEN 80, SPAN 85, MILLI Q, SEPHADEX PD10, SEP-PAKS AND BRANSON 2000 has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Regarding applicants comments on page 4 of the amendment received 8/1/95, the relationship between a trademark and the product it identifies is sometimes indefinite, uncertain and arbitrary. The characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark. See Ex Parte Simpson and Roberts, 218 USPQ 1020 and MPEP 608.01(V). Therefore it is necessary to define the trademarked reagent in term of the appropriate generic terminology.

17. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first

paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to for the reasons discussed in paragraph 20, sections A-E of the Office Action mailed 1/26/95.

18. Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification. Applicants arguments have been considered and deemed not persuasive. Publications that were not submitted with the instant amendment or which were not already of record on a PTO-892 were not considered (eg. applicants reference to the Physicians Desk Reference on page 12, of the amendment received 8/1/95).

Regarding section A, The specification does not disclose how to use the instant invention for the treatment of HCV infection in humans. Applicants arguments have been considered and deemed not persuasive. Applicant has not enabled the breadth of the claimed invention in view of the teachings of the specification. The specification has provided no evidence that instant invention can be used to treat HCV infection in humans. Applicants have provided no evidence that the chimpanzee model used in the specification predicts that the antibodies of the instant invention can be used in treating HCV infection in humans. Regarding applicants comments in pages 5-10 of the amendment received 8/1/95, the following comments are made.

Weiner et al. (1992) teach that antibodies against a peptide encompassing a peptide recited in the claims which were found in an HCV infected individual (see Abstract). However, the presence of said antibodies had no effect on HCV infection in this individual. It is unclear how this finding can be reconciled with the data in the specification derived from the single in vivo experiment that was performed with a single baboon.

The specification teaches (on page 43, last line) that the serum protein thyroid binding globulin (TBG) binds to "two minimum epitopes, one of which encompasses the SLF--G motif.". The "SLF--G motif" refers to the motif bound by the claimed antibodies. As a consequence, when the antibodies of the instant invention were administered in vivo, they would not be able to bind to the claimed conserved amino acid motif, because said motif would have been already bound by the aforementioned TBG. It is unclear whether such binding is found in the baboon model, therefore it is unclear whether the baboon model would predict whether the instant invention could be used for the treatment of human disease. It is also unclear as to how any conclusion about the activity of a therapeutic experiment can be derived from an experiment which uses one animal and no negative controls. In addition, HCV is not a naturally occurring virus in baboons. No evidence has been provided that the baboon immune response in HCV infected baboons is analogous to that seen in humans, or that humans would not possess different immune responses such that the baboon would not represent the immune response to HCV seen in humans.

Regarding applicants comments on page 12, second and third paragraphs, there is no evidence of record that HCV infection has ever been treated in humans with passive immunization. None of the claims under consideration read on a method of treating HBV. Furthermore, other viruses (such as HIV) have been refractory to antibody treatment (see Fahey et al., entire document). Applicants have provided no evidence that the method of the instant invention can be used to treat baboons that are infected with HCV prior to treatment with the instant invention. The claims as currently written encompass a method which would include the treatment of HCV infected individuals after HCV infection. This is the only use for passive immunization that is known in the art (eg. use after infection).

Regarding section B, applicants have provided no evidence that

any particular antibody preparation against any of the particular amino acid sequences recited in claims 1-5 could be used in the method of the instant invention. Applicants arguments have been considered and deemed not persuasive. Applicants comments in the letter received 1/25/94 indicates that the formula recited in claims 1 and 2 encompasses a minimum of 56,000 different peptides (see page 3, first paragraph). Applicants have provided no evidence that any particular antibody against any of these peptides can be used to treat HCV infection in any individual infected with any isolate of HCV. Weiner et al. (1992) teach that antibodies against a peptide encompassing the peptide recited in claims 1 and 2 which was derived from an HCV infected individual, do not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide is still encompassed by the formula recited in claims 1 and 2 (page 305, first paragraph). Therefore, it seems unlikely that antibodies against any particular peptide recited in said claims would bind any particular HCV isolate other than a strain with the same amino acid sequence as used to prepare said antibody. In addition, applicant has provided no evidence that all of the at least 56,000 peptides encompassed by the formula recited in claims 1 and 2 are immunogenic, and can result in the production of antibodies which bind any strain of HCV. Regarding applicants comments on page 13, the baboon data disclosed in the specification involves the use of 1 peptide out of the minimum of 56,000 different peptides encompassed by the formula recited in the claims.

Regarding section C, applicants have provided no evidence that antibodies against the peptides recited in claims 1-5 can be used in the method of the instant invention. Applicants arguments have been considered and deemed not persuasive. The chimp treated in Example 3, was treated with antibody against a 30-mer peptide. Applicants have provided no evidence that the antibodies that are responsible for whatever putative result was seen upon immunization

of said chimp were necessarily derived from the peptides recited in claims 1-5. As applicants point out in the specification (page 13, paragraph four), antibodies recognize epitopes consisting of 3 to 5 amino acids. Applicants have provided no evidence as to the specificity of the antibodies contained in the polyclonal antisera against the 30-mer peptide that are actually responsible for whatever putative result was seen upon immunization of said chimp with said antisera. Regarding applicants comments in the amendment received 8/1/95 on page 17, Example 2 in the specification deals with the immune response of goats immunized with a 30-mer peptide. There is no data in the specification indicating that the immune response of baboons would be the same as goats. There is also disclosure in the specification as to which antibodies in the polyclonal antisera against the 30-mer are responsible for whatever result is seen in the single baboon immunized in the single in vivo experiment disclosed in the specification. Furthermore, applicants have provided no evidence that antibodies against the 30-mer do not recognize a conformational epitope not contained in the peptides recited in claims 1 and 2. Therefore, the specification is not enabling for the instant invention.

Regarding section D, applicants have presented no evidence that any peptide other than the 30-mer peptide disclosed in Example 3 of the specification can be used to produce the antibody used in the method of the instant invention and achieve the putative results disclosed in Example 3 in the specification. Applicants arguments have been considered and deemed not persuasive. Applicants have not identified the putative immunoprotective epitope recognized by the antibodies raised against the intact 30-mer peptide. Applicants have no evidence to whether said epitope is linear or conformational. Therefore it is unclear as to what region of E2HV could be used an immunogen to produce the antibodies used in the method of the instant invention other than the intact 30-mer.

Regarding section E, applicants have presented no evidence that the antibody used in Example 3 of the specification can be used to prevent HCV when the recipient of the antibody is exposed to any HCV strain other than the strain used in Example 3. It is unclear that the antisera used in Example 3 will bind any HCV strain other than the particular strain used in said experiment. Weiner et al. (1992) teach that antibodies against a peptide encompassing the peptide recited in claims 1 and 2 which was derived from an HCV infected individual, do not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide is still encompassed by the formula recited in claims 1 and 2 (page 305, first paragraph). Therefore, it seems unlikely that antibodies against any particular peptide recited in said claims would bind any particular HCV isolate other than a strain with the same amino acid sequence as used to prepare said antibody. Regarding applicants comments on page 18, first paragraph, there is no evidence provided in the specification that any one particular antibody against a peptide recited in the claims binds any other peptide encompassed in the formula. In fact, Weiner et al. teaches the opposite (eg. an antibody against a peptide encompassing the peptide recited in claims 1 and 2 which was derived from an HCV infected individual, does not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide is still encompassed by the formula recited in claims 1 and 2).

19. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter

> sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

20. Claims 1-12 remain rejected under 35 U.S.C. § 103 as being unpatentable over Ralston et al. (WO 92/08734) in view of Houghton et al.(WO 90/11089).

Applicants arguments have been considered and deemed not persuasive. Ralston et al. teach that regarding the E2 antigen (which contains the conserved amino acid sequence recited in claim 1) that, "Immunogenic compositions may be administered to animals to induce production of antibodies, either to provide a source of antibodies or to induce protective immunity in the animal." (page 15, lines 15-19). The animal immunized with intact E2 antigen would produce a polyclonal antisera containing antibodies against any and all immunogenic epitopes expressed on said molecule (eg. including the conserved motif recited in claim 1). Claim 1 as currently written reads on a method using an antibody composition "comprising" an antibody capable of binding to a conserved amino acid. Therefore, the mixture of antibodies as produced by immunization with E2 antigen which contains antibodies against the conserved amino acid sequence recited in claim 1 would constitute prior art, because the claim as currently written does not read on a composition which only contains antibodies against the conserved amino acid sequence recited in the claims.

OTHER REJECTIONS

21. The following new ground of rejection were necessitated by applicants amended claims.

22. The specification is objected to under 35 U.S.C. § 112, first paragraph because the specification, as originally filed, does not provide support for the invention as now claimed.

There is no support in the specification as originally filed for the "conserved amino acid sequence" recited in claim 1 or 7. The specification does disclose a conserved "motif of amino acids" (for example see page 7, last paragraph). However, the conserved "motif", refers to a conserved pattern of amino acids, not a particular conserved amino acid sequence.

23. Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

24. No claim is allowed.

25. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD,

THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

26. Papers related to this application may be submitted to Group 180 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 180 at (703) 305-7401.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms Margaret Moskowitz Parr can be reached on (703) 308-2454. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

Ron Schwadron, Ph.D.
Patent Examiner
Art Unit 1816
October 31, 1995

DONALD E. ADAMS
PRIMARY EXAMINER
GROUP 1800